

## **REMARKS**

Claims 1, 7, 8, 19, and 20 have been amended herein. Claims 26-33, 38-40, 46-53, and 59-63 were previously canceled. Claims 1-25, 34-37, 41-45, 54-58 are pending in the application. Favorable reconsideration is respectfully requested.

Claims 1, 7, 8, and 20 have been amended in accordance with the Examiner's recommendations (as discussed more fully in the following paragraphs). Claim 19 has been amended to depend from Claim 18 (rather than Claim 13). No new matter is added.

### **Allowed and Allowable Subject Matter:**

Applicants note with thanks the indication that Claims 17, 18, 43-45, and 54-58 have been allowed outright.

Applicants also note with thanks the indication that Claims 1-12, 20-25, and 34-36 contain allowable subject matter. The amendments made herein are believed to place these claims into condition for allowance.

### **Objections to Fig. 1:**

Submitted herewith is a substitute Fig. 1. Entry of the substitute figure is respectfully requested.

Applicants note that the "tryptase  $\alpha$ " sequence shown in Fig. 1 is depicted in SEQ. ID. NO: 52. The remaining depictions in Fig. 1 are merely to designate the positions and nature of the various differences in amino acid sequence between "tryptase  $\alpha$ " and "tryptase  $\beta$ -I" and "tryptase  $\beta$ -II." Applicants respectfully submit that the various designations in Fig. 1 under the headings "tryptase  $\beta$ -I" and "tryptase  $\beta$ -II" are not subject to the sequence rules of 37 CFR §1.821 because these sections of the figure do not depict unbranched amino acid sequences of four or more amino acid residues. The full-length  $\alpha$  sequence, of course, is subject to the sequence rules and is therefore presented in SEQ. ID. NO: 52. Thus, in the substitute Fig 1 submitted herewith, the sequence identification references to SEQ. ID. NOS: 6 and 9 have been removed.

**Rejection of Claims 1-6, 7-12, 20-25, and 34-36 Under 35 USC §112, Second Paragraph:**

This rejection is believed to have been overcome by appropriate amendment to the claims, in accordance with the Examiner's recommendations.

Specifically, Claims 1, 7, and 8 have been amended to recite the positions of the mutated amino acid residues with respect to the polypeptide sequences shown in Fig. 1, as suggested by the Office in the Final Office Action.

Claim 20 has been amended to recite a "method of producing enzymatically inactive proteolytic tryptases...."

In light of the amendment to the claims, Applicants submit that the rejection of Claims 1-6, 7-12, 20-25, and 34-36 under 35 USC §112, second paragraph has been overcome. Withdrawal of the same is respectfully requested.

**Rejection of Claims 13-16, 19, 37, and 41-42 Under 35 USC §112, First Paragraph (Written Description & Enablement):**

As applied to Claim 19, this rejection is believed to have been overcome by amending Claim 19 to depend from Claim 18.

As applied to Claims 13-16, 37, and 41-42, these two rejections are respectfully traversed. Because the rejections are closely related, they shall be addressed simultaneously.

The Office's characterization of Claim 13 at the bottom of page 5 of the Office Action is absolutely correct. Claim 13 is directed to a DNA construct which comprises a genus of DNAs encoding any proteolytic tryptase having any mutation in the active site. This is Applicants' intent. Applicants respectfully submit that Claim 13 (as well as the other claims made subject to these rejections) does not run afoul of either the written description requirement or the enablement requirement because the specification clearly exemplifies proteolytic tryptases having mutations in the active site, and clearly enables how to make such mutations. Thus, it is respectfully submitted that the invention has been described and enabled to the level required by §112.

Regarding the nature of tryptases, Applicants respectfully point out that the Office's comments at the top of page 6 of the Final Office Action cut in Applicants' favor. Here, the Office states "tryptases are known to be tetrameric enzymes." As far as Applicants can determine, all enzymatically active tryptase now known are tetrameric - a fact that supports Applicants' position that a description of one member of the genus is sufficient to describe and to enable all of the species falling within the genus (because of their structural similarity). See also Exhibit A submitted with Applicants' earlier response..

In terms of the written description requirement of §112, first paragraph, the genus of expression constructs recited in Claim 1 is thus disclosed verbatim in the application as filed, as evidenced by the sequences depicted in Fig. 1, and recited in the Sequence List, most notably at SEQ. ID. NOS: 6, 9, 21, 23, 25, 27, 37, 39, 41, 43 and 52. See also the list of suitable promoter/terminators at page 18, last paragraph of the specification. See also Table 1 (starting at page 35 of the specification) which lists the various mutants that were actually fabricated, inserted into a construct as now claimed, cloned into a yeast host, and the mutant tryptases encoded thereon expressed. Some of these tryptases were even isolated and characterized. See the Examples, especially starting at page 40.

In short, the written description and enablement requirements of §112 require only that Applicants describe how to make and use the invention commensurate in scope with the claim language. Applicants submit that this has been done by describing a general approach for making active site mutants of various tryptases and exemplifying several working versions of the mutants.

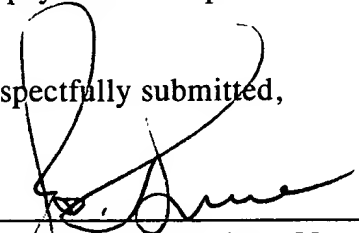
For these above reasons, Applicants submit that this rejection under §112, first paragraph (written description and enablement) is improper. Withdrawal of the rejection is respectfully requested.

### **CONCLUSION**

In light of the above amendments and accompanying remarks, Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited.

The Commissioner is hereby authorized to charge any additional fees or credit any overpayment to Deposit Account No. 18-2055.

Respectfully submitted,



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**Joseph T. Leone, Reg. No. 37,170**  
DEWITT ROSS & STEVENS S.C.  
8000 Excelsior Drive, Suite 401  
Madison, Wisconsin 53717-1914  
Telephone: (608) 831-2100  
Facsimile: (608) 831-2106